rest, explain its relationship to the present condition and by a number of constructive talks reestablish the former state of confidence.

In the study of even mild cases of mental disturbance new light is thrown on the causes of and peculiarities in human conduct. In normal persons the mechanisms which determine the flow of ideas are under control; the natural and acquired inhibitions are functioning in proper sequence and the emotions are held in check by a consciously acting intelligence. But with mental imbalance there is a lack of coördination between the intelligence and the emotions. Inhibitions are either overactive or cease to be the guardian sentinels of thought and conduct. The hidden springs which supply the stream of consciousness are uncovered and the motives which determine behavior stand out in bold relief. To the mental patient is well applied the words of Prospero,

"Thy nerves are in their infancy again,
And have no vigor in them."

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REFERENCES

1. Bolton, Joseph Shaw. Sixth Maudsley Lecture. J. Ment. Sc., July 1925.
2. Mackay, Charles, LL.D. Memoirs of Extraordinary Popular Delusions and the Madness of Crowds. London, 1852.

LATE SYPHILIS—TREATMENT WITH A SINGLE STRAIN OF MALARIA*

ANALYTICAL EVALUATION OF THERAPEUTIC RESULTS IN FOUR HUNDRED CASES

By Ross Moore, M. D.
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Discussion *by Henry G. Mehrtens, M.D., San Francisco; Walter E. Leonard, M.D., Los Angeles.*

THE clinical course of syphilis after its secondary manifestations have disappeared is curiously vague and uncertain. Therefore the therapeutics of this period are necessarily in a corresponding state of conceptual chaos. It is therapy without clear foundational thought—treatment without adequate biological substratum.

STATISTICAL STUDY OF FOUR HUNDRED CASES

This analysis is an effort to think back toward physiological origins via malaria therapy.

Three hundred and fifty of the cases in this series were diagnosed paresis. Fifty of them were tabes or cerebro spinal syphilis.

Two hundred and thirty-four of the paretics were treated in Norwalk State Hospital between December, 1926, and December, 1929.

Dr. F. J. Van Meter, resident syphilologist, has made a statistical study of this series as of May 1, 1930—four months after the last treatment had been finished. He reports as follows: sixty-eight patients or 29 per cent improved sufficiently to be paroled or discharged; fifty-nine or 25 per cent improved markedly but are still in the institution; forty-one or 17 per cent are unimproved; sixty-six or 28 per cent died during or shortly after treatment.

In discussing these results Doctor Van Meter calls attention to the fact that remissions occur in only three or four per cent of untreated paretics and in six or seven per cent of those treated with arsenicals. Although statistics of this kind are unreliable things, yet Doctor Van Meter's percentages warrant the conclusion that at Norwalk at least, malaria treatment in paresis has been more helpful than other methods.

Throughout the world many thousand treatments of this kind have been given during the last thirteen years. Some investigators are enthusiastic in favor of malaria treatment. Others are conservative. None have condemned it wholesale. But the method cannot yet be said to have entirely proved itself. This it may do in the future. Again it may not. Even though finally discarded, malaria treatment will have been extremely useful in helping to clarify and advance anti-syphilitic therapeutics.

During this study of the effects of malaria in syphilis the need for a more scientific sense of human physiology in action against Treponema, has been keenly felt. Standard accepted therapeutic methods against syphilis are empiric in theory, or have no theory. This makes them inadequate in practice. They neither kill treponemic infection nor prevent recrudescences, a bitter and humiliating admission.

A theory of treatment is needed which has for its basis the physiology or physio-pathology of syphilis. This would be a live theory. The present theory, based upon symptoms and pathologic findings is a dead theory.

STAGES IN PHYSIOLOGIC PROGRESS IN SYPHILIS

So far as its reaction on human physiology is concerned, syphilis divides itself into five stages or periods, viz., primary and secondary syphilis as in the old classification, hidden syphilis, irritative syphilis and degenerative syphilis.

For use in this present study these periods may be sketched as follows:

Primary syphilis possesses but one lesion, the external evidence of that vigorous effort which physiological defense mechanisms are making to prevent generalized invasion of the body by Treponema pallidum. Defense mechanisms may hinder such invasion but seldom or never prevent it.

Thus general systemic invasion soon becomes a reality and the second period, called secondary syphilis, has begun. Its cutaneous, neural and other manifestations are the visible evidence that defense mechanisms are being forced to wage a desperate defensive warfare in every part of the body.

The gradual disappearance of these secondaries indicates that defense mechanisms have become strengthened gradually until a fighting ability somewhat near equal to that of Treponema has been attained.

* Read before the General Medicine Section of the California Medical Association, at the Fifty-ninth Annual Session, Del Monte, April 28-May 1, 1930.

When this equality is attained and has become stabilized, the third period called hidden syphilis replaces the second period. Hidden syphilis lasts exactly as long as defense mechanisms maintain their fighting equality with Treponema. However, during this entire pseudo quiescent period, burrowing, sapping, enervating syphilitic attrition never ceases.

After months or years, trouble breaks out again. Signs and symptoms now indicate that defense is crumpling and breaking before treponemic onslaught. It is the beginning of the fourth period, called irritative syphilis. This period lasts a long or a short time, depending on whether the patient possesses powers of resistance that are hereditarily great or small.

Sooner or later the period of irritative syphilis is crowded out by the fifth period, degenerative syphilis. Thereafter the clinical course of the disease is slowly materializing death.

For the sake of greater clarity, these five physiologic periods are restated in epitomized form as follows:

In primary syphilis, strong but inexperienced physiologic defense mechanisms try unsuccessfully to prevent a local treponemic infection from becoming generalized.

In secondary syphilis, stronger and more experienced defense mechanisms fight Treponema in all parts of the body, with considerable success.

In hidden syphilis, still stronger and more experienced defense mechanisms prevent for the time being the appearance or reappearance of all syphilitic symptomatology.

In irritative syphilis, defense mechanisms begin to show signs of exhaustion. New signs and symptoms then make their appearance.

In degenerative syphilis, defense mechanisms have become destroyed and are dead.

Primary and secondary syphilis constitute an inclusive classification called early syphilis. Irritative and degenerative syphilis are late syphilis. Hidden syphilis is a transitional period.

At some time during the transitional period of hidden syphilis a physio-pathologic turning point is reached. Previous to it, defense mechanisms are strong and able. After the transitional period they gradually lose strength and ability until death closes the scene. This is also a moment when a change of method must be made if therapy is to adequately meet new conditions. The kind and quality of therapeutic help required after the turning point is quite different from that needed before it. Afterward, the human mechanism requires support and revitalization above everything else.

THEORY OF THERAPY BY MALARIA IN LATE SYPHILIS

Does malaria treatment in any way meet this requirement? Does it support and revitalize failing defense mechanisms?

Statistics in general and those of Norwalk in particular seem to answer these questions in the affirmative, in so far as paresis is concerned. The following case appears to affirm it for tabes.

A fifty-two year old barber contracted syphilis thirty-two years ago. Lightning pains began sixteen years ago and thereafter a typical clinical picture of tabes developed in spite of well applied standard therapy.

Fifteen months ago this patient was given malaria treatment. Straightway his lightning pains disappeared and have not reappeared. He became physically a great deal stronger and lost much of his ataxia. For the last ten months he has been back at his trade, although still somewhat ataxic and quite devoid of knee jerks and pupillary reflexes.

It is reasonable to believe that in this case syphilitic irritation of the spinal cord has been negatived or neutralized or abolished by malaria treatment.

If space permitted, favorable results in many varieties of cerebro-spinal syphilitic involvement might be cited.

It is therefore possible to answer the above questions in the affirmative. Malaria treatment *is* able to support and revitalize physiologic defense mechanisms in many different types of late syphilis.

Granting that malaria treatment is effectual, how does it accomplish this feat?

Apparently it causes a decrease in syphilitic irritation, although the ultimate biochemical *modus operandi* by which it does this is unknown. Possibly there is some significance in the fact that the treponemic cause of syphilis is first cousin to the plasmodial cause of malaria, although the activities of these cousins, inside the body, seem very different. Treponema attacks sluggishly and ponderously. Plasmodium attacks violently and spectacularly. It thus results that physiologic defense mechanisms are stirred into much more immediately vigorous and aggressive action by plasmodium than by Treponema. Is it possible that antibodies formed by plasmodial energeticalness are more potent against Treponema than those formed by Treponema itself?

However this may be, one fact begins to be clear— malaria treatment is a distinctly physiological type of remedy. It apparently accomplishes its object by stimulating or aiding the natural defenses of the body to reassume their normal tasks.

Another question—

If malaria treatment has done so much for certain types of late syphilis, what other things may it be able to accomplish?

The answer is, that malaria treatment may be useful wherever there is gradually developing syphilitic weakness. This is a broad statement but a justifiable one. During all of irritative and degenerative syphilis, gradually developing weakness is present. The period of degenerative syphilis is included here, not because it is amenable to any form of treatment but because it is clinically inseparable from irritative syphilis. Only therapeutic test can disclose whether a given case is irritative syphilis or degenerative syphilis or a mixture of the two. Most cases which show fairly

completely developed clinical pictures of paresis and tabes are this kind of mixture.

It would be somewhat daring to say that malaria treatment should be used in hidden syphilis. It would be more daring to say that it should be used in secondary syphilis. It would be most daring to say that it should be used in primary syphilis. There is no present warrant for such statements. But there is not only warrant but sound common sense in the idea that the use of malaria treatment should be considered wherever and whenever physiologic defense mechanisms give signs of failure in their struggle against syphilis.

Compare the use of this physiologically supportive remedy to the fatuous and futile drenching of slipping patients with synthetic, metallic proprietaries.

VALUE OF COMBINATION OF OLD AND NEW THERAPY

Other questions present themselves in this connection. For example, what is the best way to combine old therapy with new therapy in late syphilis, or should they be combined? How many malarial paroxysms should be allowed? How soon, if ever, should malaria treatment be repeated? and so forth.

Answers would be interesting to work out but would carry this discussion too far afield from its primary object. Enough has been said to focus attention and stimulate interest in the physiologic reactions of the human body when invaded by Treponema. Clear thinking along this line will result in better engineered anti-syphilitic treatment.

Four hundred cases are not enough to prove a point. Neither do forty-odd months of experience with a particular method of treatment prove its quality. Nevertheless, when those cases and that method are reviewed before the limitless background of historic syphilology, a conclusion, an impression and a concept, are left in mind.

The conclusion: Malaria treatment with the occasional aid provided by older therapeutic procedures, is the best method at present available for combating late syphilis.

The impression: The physiologic aptness of malaria treatment in late syphilis gives the therapist a sense of solid satisfaction and accomplishment which has never before been experienced in connection with the older methods.

The concept: In order to be adequately understood, late syphilis must be conceived of as a period in which physiological defense mechanisms are fighting an uncertain and apparently a losing engagement with Treponema. Therefore, the supremest possible therapeutic accomplishment of the moment is to adroitly support and revitalize these struggling defense mechanisms in this their final life and death combat.

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DISCUSSION

HENRY G. MEHRTENS, M. D. (Stanford University Hospital, San Francisco).—Dr. Ross Moore's paper is exceedingly timely. We need to be continually reminded that we have not the faintest notion of how our arsenic, mercury, or bismuth affects the spirochetes. Neither have we any accurate method of judging just what dosage is helping the organism in its fight with the spirochetes, and what dosage may actually be handicapping the patient in his struggles. We must be ever on the alert to utilize our best clinical judgment to see that we do not overwhelm the bodily defenses with our medications. That malarial treatment helps neurosyphilis not amenable to the ordinary intensive antiluetic medication must be admitted by all who have had any considerable experience with the method. There is some doubt in my mind that the malarial treatment will be our ultimate solution of the problem. At Stanford we have utilized the fever produced by baths—104 degrees to 106 degrees Fahrenheit mouth temperature—with results comparing well with those we secured with malaria. Other clinics have used fevers produced by electricity.

Fever alone may not be all that is necessary; other factors may have to be added. We are convinced that the ordinary antiluetic medication is far more effective in the presence of fever. But whatever may be the method of treatment, we are now in possession of an additional means of attack upon the spirochete, as Dr. Ross Moore has so well pointed out, in harmony with the physiological defenses of the body. It will not only achieve clinical results not obtainable by the older methods, but may be used to reinforce and amplify intensive antiluetic therapy. We may anticipate many further advances along these lines.

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WALTER E. LEONARD, M. D. (520 West Seventh Street, Los Angeles).—Doctor Moore is to be congratulated for bringing to our attention the physiological basis underlying the treatment of late syphilis by malaria therapy.

To review briefly, fever may be induced by various substances other than bacterial or parasitic toxins, viz., drugs such as cocain, certain purins, sugars and diuretics. In these conditions the fever causes a breaking down of tissue cells and increases the osmotic pressure of their protoplasm, and water is therefore attracted into them from the blood, resulting in an increased concentration of the circulating blood. Whereas, an upset of the heat regulating centers of the brain by external heat or electricity will also cause a rise in temperature without change in the concentration of the blood.

Reasoning from the above physiological basis, there seems to be no foundation for the thought that malaria therapy in late syphilis is in any way specific and possible improvement might be attained by other substances.

Persistence in the use of certain synthetic, metallic proprietaries are no doubt indicated in the first stages of syphilis, serving to stimulate the defense mechanisms of the body against the generalized invasion of Treponema pallidum. This defense mechanism may be maintained for years under careful management, but once degenerative changes have occurred the method of attack must be changed as indicated in Doctor Moore's paper.

IMMUNIZATION AGAINST DIPHTHERIA WITH TOXIN-ANTITOXIN*

By H. E. THELANDER, M. D.
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AT the health center conducted by the American Association of University Women, located on Oak Street, San Francisco, it has been a part of the routine the past several years to immunize baby patients against diphtheria, and to vaccinate against smallpox, before graduating the child to the runabout class at the age of eighteen months.

* From the department of pediatrics University of California and Children's Hospital. Accepted March, 1930.